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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/662,820	09/16/2003	Yukihiro Koike	1089.0410001/TUM	1102

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EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/662,820	KOIKE ET AL.	
	Examiner	Art Unit	
	Raymond J Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-15 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-15 is/are rejected.

7)☒ Claim(s) 10-12 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on January 12, 2004 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 5/7/2004.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

CLAIMS 1-15 ARE PRESENTED FOR EXAMINATION

Applicants' Information Disclosure Statement filed May 7, 2004 has been received and entered into the application. As reflected by the attached, completed copies of form PTO/SB/08a (2 pages), the cited references have been considered.

Claim Objection

Claims 10-12 are objected to because of the following informalities:

In claim 11, the claimed objective is inhibiting the recurrence of hepatocellular carcinoma and such would require a previous occurrence of said carcinoma. This is not, however, reflected by the mere recitation of "a patient" at line 2.

Claim 11 should be amended by inserting ---who has suffered from said carcinoma--- (or other appropriate language) after "patient" in order to overcome this objection.

For reasons analogous to those above respecting claim 11, the patient of claims 10 and 12 should also be amended to reflect the patient's status. That is, in claims 10 and 12, ---in need thereof--- should be inserted after the term "patient".

Claim Rejection - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 13 and 14 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*,

255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejection - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 10 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating a hepatic disease or inhibiting the occurrence of portal venous invasion, does not reasonably provide enablement for preventing a hepatic disease or portal venous invasion. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The burden of enabling the prevention of a hepatic disease or portal venous invasion would be much greater than that of enabling the treatment of a hepatic disease or portal venous invasion. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing a hepatic disease or portal venous invasion or how a patient could be kept from every being susceptible to these conditions. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for preventing a hepatic disease or portal venous invasion.

Specifically, it is highly unlikely, and the Office would require experimental evidence to support the contention that the claim specified active could actually prevent a hepatic disease or portal venous invasion by simply administering, by any method, an amount of the claim specified active agent. The specification fails to enable one of ordinary skill in the art to practice

the prevention of a hepatic disease or portal venous invasion.

The term "prevention" or "preventing" is synonymous with the term "curing" and both circumscribe circumstances of absolute success. Since absolute success is not reasonably possible with most diseases/disorders, especially those having etiologies and pathophysiological manifestations as complex/poorly understood as a hepatic disease or portal venous invasion, the specification, which lacks a showing that any hepatic disease or portal venous invasion is actually prevented, is viewed as lacking an adequate written description of the same. At Figure 3, applicants have demonstrated that the incidence of portal venous invasion can be inhibited. However, such does not establish that the claimed active agent actually prevents portal venous invasion.

Accordingly, the claims are deemed properly rejected.

Suggestion for Overcoming the Rejection

In order to overcome the present rejection, it is suggested that "preventing" in claims 1 and 15 be deleted. In claim 10, it is suggested that "preventing" be changed to ---inhibiting the occurrence of portal venous invasion---.

Claim Rejection - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13 and 14 provide for the use of menatetrenone for manufacturing an agent and inhibiting recurrence of hepatocellular carcinoma, respectively. However, because the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicants are intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I Claims 1-9, 13 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Ida et al. (U.S. Patent No. 5,021,570) who teach a pharmaceutical composition comprising menatetrenone as an active agent as well as a method for manufacturing the composition (see the abstract, Examples 1-5 at cols. 3-5 (manufacturing process) and Table 1 at cols. 5-6 (compositions).

The statements of intended use or mechanism of action in the present claims that are not disclosed in Ida et al. are noted, but not given patentable weight because such statements do not impart any physical or otherwise material feature to the claimed composition that is not found in the compositions taught by the Ida et al. Applicants' attention is directed to In re Dillon, 16 USPQ2d 1897 at 1900 (CAFC 1990) where it was held that the recitation of a new utility for an

old and well known composition does not render that composition new.

II Claims 1-9 and 11-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Furukawa et al. (cited by Applicants, cit. ref. "AB2") and STN Registry file Monograph of RN 863-61-6 ("STN Monograph", secondary reference cited only to explain meaning of a term in the primary reference; see MPEP 2131.01(B)) **or** under 35 U.S.C. 102(a) as being anticipated by Koike et al. (cited by Applicants, cit. ref. "AF2"; considered to by "by others" because the inventive entity of the reference is different than that of the instant application) taken with applicants' acknowledgment at page 7, lines 3-4; relied upon to show the meaning of term (MPEP 2131.01(B)).

Furukawa et al. teach that the administration of menaquinone-4 (a.k.a. menatetrenone; see STN Monograph at lines 4 and 6 following the heading "OTHER NAMES"; also a "vitamin K" compound required by present claim 15; see the Monograph at line 8 under the same heading) to patients suffering from hepatocellular carcinoma was effective to decrease the patients' plasma, i.e., blood, level of des-gamma-carboxy prothrombin (present claim 12). Compositions of menaquinone-4 containing 50 mg. and 10 mg. are also taught. See the abstract at page 31 and the entirety of page 32.

Koike et al. teach that the administration of vitamin K-II (a.k.a. menatetrenone; see the present specification at page 7, lines 3-4) to patients suffering from hepatocellular carcinoma was effective to inhibit portal venous invasion (PVI). Oral compositions of vitamin K-II (45mg/day) are also taught.

Concerning claims 1-9 and 15, which are directed merely to "an agent", the statements of intended use or mechanism of action in these present claims that are not disclosed in the

reference are noted, but not given patentable weight because such statements do not impart any physical or otherwise material feature to the claimed composition that is not found in the compositions taught by the Ida et al. Applicants' attention is directed to In re Dillon, 16 USPQ2d 1897 at 1900 (CAFC 1990) where it was held that the recitation of a new utility for an old and well known composition does not render that composition new.

In present claims 11 and 14, applicants have claimed methods of inhibiting recurrence of hepatocellular carcinoma that require the administration of an effective dose of menatetrenone to a patient. Furukawa et al. and Koike et al. disclose each and every one of the claim limitations except the objective of inhibiting the recurrence of hepatocellular carcinoma. However, because the references teaches that the same active agent is administered to the same patient and in effective amounts as in the present claims, the claimed objectives must be inherent in the prior art method whether expressly disclosed or not.

Claim 10 is not subject to the present rejection because Furukawa et al. fail to teach the prevention of PVI and Koike et al. merely teach the inhibition of PVI.

Legal Standard for Anticipation/Inherency Under - 35 USC § 102

To anticipate a claim under 35 U.S.C. 102(b), a single prior art reference must place the invention in the public's possession by disclosing each and every element of the claimed invention in a manner sufficient to enable one skilled in the art to practice the invention. *Scripps Clinic & Research Foundation v. Genetech, Inc.,* 927 F.2d 1565, 1576, 18 U.S.P.Q.2d 1001, 1001 (Fed. Cir. 1991); *In re Donahue,* 766 F2d531, 533, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985). To anticipate, the prior art must either expressly or inherently disclose every limitation of the claimed invention. *MEHL/Biophile Int'l Corp. v. Milgraum,* 192 F.3d 1362, 1365, 52

U.S.P.Q.2d 1303, 1303 (Fed. Cir. 1999) (citing to *In re Schreiber,* 128 F.3d 1473, 1477, 44 U.S.P.Q. 1429, 1431 (Fed. Cir. 1997)); *Atlas Powder Co. v. Ireco Inc.,* 190 F.3d 1342, 1347, 51 U.S.P.Q.2d 1943, 1946 (Fed. Cir. 1999). To inherently anticipate, the prior art must necessarily function in accordance with, or include, the claimed limitations. *MEHL/Biophile*, 192 F.3d at 1365, 52 U.S.P.Q.2d at 1303. However, it is not required that those of ordinary skill in the art recognize the inherent characteristics or the function of the prior art. *Id.* Specifically, discovery of the mechanism underlying a known process does not make it patentable.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 and 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over (1) Furukawa et al. and the STN Registry file Monograph of RN 863-61-6 **or** (2) Koike et al. and applicants' acknowledgment at page 7, lines 3-4, as above, for not only the reasons above and

because anticipation is the epitome of obviousness, but also in view of applicants' acknowledgment in the specification at page 7, lines 1-5 and Wang et al. (cited by applicants cit. ref. "AD2").

If not inherently disclosed, a difference between the above and the claimed subject matter would lie in that none of the references disclose that the recurrence of hepatocellular carcinoma could be inhibited (present claims 11 and 14).

However, to the skilled artisan, the claimed subject matter would nevertheless have been obvious because applicants acknowledge that the claimed compound "menatetrenone" was a known vitamin K compound and Wang et al. teach that the vitamin K compounds inhibit the growth of hepatocellular carcinoma "HCC" (abstract at page 876, first and last line and page 880-881 under the heading "Discussion"). The skilled artisan would have been motivated to employ menatetrenone to inhibit the recurrence of HCC because of menatetrenone's known anti-HCC characteristics as taught by Wang et al. and the desire to not have a patient who has previously suffered from hepatic cancer not to suffer from that cancer again.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Raymond J Henley III
Primary Examiner
Art Unit 1614

November 12, 2004